AMENDMENTS TO THE CLAIMS:

Please replace the claims with the claims provided in the listing below wherein status, amendments, additions and cancellations are indicated.

1. (Currently Amended) A method of deriving blood perfusion indices for a region of interest (ROI) of a subject, the method comprising the steps of:

administering a contrast agent to the subject during a dynamic imaging scan:

converting signal intensity data from raw images of the scan into contrast agent concentration data;

deriving parameters from the contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent, wherein the at least one transport function includes an arterial transport function $h_a(t)$ represented by a first model through a vessel leading to the ROI; and

calculating the blood perfusion indices from the derived parameters.

2-3. (Cancelled).

4. (Currently Amended) A method according to claim [[3]] 1, wherein the at least one transport function further comprising using a second model to represent comprises a tissue transport function $h_s(t)$ represented by a second model through the ROI.

5. (Currently Amended) A method according to claim [[4]] 1 further comprising the step of selecting an arterial input function $AIF_a(t)$ in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.

6. (Original) A method according to claim 5 further comprising the step of measuring the contrast agent concentration $C(t)$ remaining in the ROI.

7. (Currently Amended) A method according to claim [[6]] 1 further comprising the step of representing $h_a(t)$ using a gamma-variate function (GVF) in the first model such that:

$$h_a(t) = \begin{cases} \dfrac{1}{A_1}(t-t_1)^{\alpha_1} e^{-(t-t_1)/\sigma_1} & (t \geq t_1) \\[2em] 0 & (t < t_1) \end{cases}$$

where $A_1 = \sigma_1^{1+\alpha_1}\Gamma(1+\alpha_1)$, $\Gamma(\alpha) \equiv \int_0^\infty x^{\alpha-1}e^{-x}dx$ is the Gamma function, t_1 is the time taken for the contrast agent to move from the initial measurement of <u>arterial input function</u> $AIF_a(t)$ to a vessel at the entry to the ROI, σ_1 and α_1 are related to the mean transit time and dispersion of $h_a(t)$.

8. (Original) A method according to claim 7 further comprising the step of estimating $h_a(t)$ after deriving values for parameters t_1 and σ_1 and setting $\alpha_1 = 0$ using the equation:

$$h_a(t) = \begin{cases} \dfrac{1}{\sigma_1} e^{-(t-t_1)/\sigma_1} & (t \geq t_1) \\ \\ 0 & (t < t_1) \end{cases}$$

9. (Currently Amended) A method according to claim [[8]] 7 further comprising the step of determining an estimate for the arterial input function $AIF_t(t)$ of the vessel at the entry to the ROI using the equation:

$$AIF_t(t) = AIF_a(t) \otimes h_a(t) \equiv \int_0^t AIF_a(\tau) h_a(t - \tau) d\tau$$

where $\otimes$ is the convolution operator.

10. (Original) A method according to claim 9 further comprising the step of determining an estimate of blood flow F_t and an estimate of the tissue IRF $R_e(t)$ from the deconvolution of:

$$C(t) = (F_t / k_H) AIF_t(t) \otimes R_e(t)$$

where $k_H = (1-H_a)/(1-H_t)$ is a correction constant taking into account different values of arterial hematocrit H_a and tissue hematocrit H_t since the contrast agent remains in the extracellular fraction of blood (plasma).

11. (Original) A method according to claim 10 further comprising the step of determining an estimate for the tissue transport function $h_e(t)$ from the estimated $R_e(t)$ using the equation:

$$h_e(t) = - \frac{d}{dt} R_e(t)$$

12 (Currently Amended) A method according to claim [[11]] 15 further comprising the step of determining a rise time and a mean transit time of $h_e(t)$ in order to determine parameters α_2 and σ_2 by assuming $t_2=0$, where t_2, α_2 and σ_2 are parameters related to the mean transit time and dispersion of ~~$h_e(t)$~~ $\underline{h_s(t)}$.

13. (Currently Amended) A method according to claim [[11]] 16 further comprising the step of determining a peak height and a mean transit time of $h_e(t)$ in order to determine parameters σ_2 and t_2 by assuming $\alpha_2=0$, where t_2, α_2 and σ_2 are parameters relating to mean transit time and dispersion of ~~$h_e(t)$~~ $\underline{h_s(t)}$.

14. (Currently Amended) A method according to claim [[12]] 4 further comprising the step of representing a ~~simulated~~ tissue transport function $h_s(t)$ using a GVF in the second model such that:

$$h_s(t) = \begin{cases} \dfrac{1}{A_2}(t-t_2)^{\alpha_2} e^{-((t-t_2)/\sigma_2)} & (t \geq t_2) \\ \\ 0 & (t < t_2) \end{cases}$$

where $A_2 = \sigma_2^{1+\alpha_2}\Gamma(1+\alpha_2)$, t_2, σ_2 and α_2 are parameters related to the mean transit time and dispersion of $h_s(t)$ through the ROI.

15. (Original) A method according to claim 14 further comprising the step of estimating $h_s(t)$ using the derived values for parameters α_2 and σ_2 by setting $t_2=0$ using the equation:

$$h_s(t) = \frac{1}{A_2} t^{\alpha_2} e^{-t/\sigma_2} \qquad (t \geq 0)$$

16. (Original) A method according to claim 14 further comprising the step of estimating $h_s(t)$ using the derived values for parameters σ_2 and t_2 by setting $\alpha_2=0$ using the equation:

$$h_s(t) = \begin{cases} \dfrac{1}{\sigma_2} e^{-(t-t_2)/\sigma_2} & (t \geq t_2) \\[4mm] 0 & (t < t_2) \end{cases}$$

17. (Currently Amended) A method according to claim [[15]] 14 further comprising the step of determining a simulated tissue IRF $R_s(t)$ using the equation:

$$R_s(t) = 1 - \int_0^t h_s(\tau) d\tau$$

18. (Original) A method according to claim 17 further comprising the step of determining a simulated contrast agent concentration $C_s(t)$ using the equation:

$$C_s(t) = (F_t/k_H) \, AIF_t(t) \otimes R_s(t)$$

19. (Original) A method according to claim 18 further comprising the step of fitting the simulated $C_s(t)$ to $C(t)$ using a least squares method according to:

$$S = \sum_t (C(t) - C_s(t))^2$$

20. (Original) A method according to claim 19 further comprising the step of optimising the parameters F_t, t_1, σ_1, α_1, σ_2, α_2 and t_2 by minimizing S iteratively.

21. (Original) A method according to claim 20 further comprising the step of reducing the number of adjustable parameters by fixing $\alpha_1 = 0$ and $t_2 = 0$, or fixing $\alpha_1 = 0$ and $\alpha_2 = 0$ leading to five adjustable parameters.

22. (Currently Amended) A method according to claim [[20]] 8 comprising the step of further reducing the number of adjustable parameters by fixing a relative dispersion, $\beta_1 = \sigma_1/(\sigma_1 + t_1)$, of $h_a(t)$ resulting in σ_1 dependent on t_1, leading to four adjustable parameters.

23. (Currently Amended) A method according to claim [[22]] 49 further comprising the step of calculating quantitative blood perfusion indices from the optimized parameters of F_t, t_1, σ_1, α_1, σ_2, α_2 and t_2.

24. (Original) A method according to claim 23 wherein the perfusion indices include any one or more of blood flow, blood volume, mean transit time, arterial delay time, arterial dispersion time or relative arterial dispersion, tissue dispersion time or relative tissue dispersion.

25. (Currently Amended) A method according to claim [[24]] 49 further comprising the step of repeating each previous step, apart from the step of selecting the AIF, on a

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pixel-by-pixel basis to produce quantitative maps of the perfusion indices for further

analysis and presentation.

26-29. (Cancelled)

30. (Original) A method according to claim [[29]] <u>5, wherein the vessel is an artery, the</u>

<u>method</u> further comprising determining a venous input function $VIF_a(t)$ from a draining

vein to estimate an $AIF_a(t)$ where a selected artery has partial voluming, the vein being

larger than the artery.

31. (Original) A method according to claim 30 further comprising the step of

determining the profile of $VIF_a(t)$ from the draining vein.

32. (Currently Amended) A method according to claim [[31]] <u>50</u> further comprising

the step of scaling $AIF_a(t)$ to have the same first-pass bolus peak area as the $VIF_a(t)$ ~~to~~

~~minimize partial voluming effect from the $AIF_a(t)$~~.

33. (Original) A method according to claim 32 wherein the first-pass bolus peak areas

of the $AIF_a(t)$ and $VIF_a(t)$ profiles are obtained by fitting the profiles to gamma-variate

function (GVF) profiles respectively to remove contrast recirculation effects.

34. (Currently Amended) A method according to claim 17 further comprising the step

of determining a simulated tissue IRF $R_s(t)$ in the case that the contrast agent does not

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always remain in the vascular system, such as in a tumour in the subject in order to

determine blood perfusion indices and permeability indices using:

$$R_s(t) = 1 - \int_0^t h_s(\tau)d\tau + Ee^{-kt}\int_0^t h_s(\tau)e^{k\tau}d\tau$$

where $h_s(t) = \begin{cases} \dfrac{1}{A_2}(t - t_2)^{\alpha_2} e^{-(t-t_2)/\sigma_2} & (t \geq t_2) \\ \\ 0 & (t < t_2) \end{cases}$;

E is the extraction fraction of the tracer in the blood stream that leaks out of the vessel

into tissue, and the tracer clearance rate constant $k = E*F_t/V_e$ is a rate constant at which

the leaked contrast agent diffuses back into the blood stream and leaves the tissue, $\underline{F_t \text{ is}}$

$\underline{\text{the blood flow and}}$ V_e is volume fraction of the extravascular and extracellular space

(EES).

35. (Original) A method according to claim [[33]] $\underline{34}$ wherein a permeability surface

area product PS is determined by $PS = -F_t \ln(1 - E)$.

36. (Previously Presented) Computer program means for deriving blood perfusion

indices for a region of interest (ROI) of a subject by directing a processor to carry out

the method steps of claim 1 apart from the step of administering a contrast agent to the

subject during a dynamic imaging scan.

37. (Original) Computer program means according to claim 36 further directing the

processor to retrieve raw image data from the dynamic imaging scan of the subject after

a contrast agent is administered to the subject.

38. (Currently Amended) A system of deriving blood perfusion indices for a region of

interest (ROI) of a subject, the system comprising:

scanning means for providing a dynamic image scan of the subject during which

a contrast agent is administered to the subject;

processor means linked to the scanning means for retrieving raw image data

from the scan;

the processor means further:

converting signal intensity data included in the retrieved raw image data into

contrast agent concentration data;

deriving parameters from the contrast agent concentration data using at least one

transport function that accounts for delay and dispersion of the contrast agent, wherein

the at least one transport function includes an arterial transport function $h_a(t)$

represented by a first model through a vessel leading to the ROI; and

calculating the blood perfusion indices from the derived parameters.

39-40. (Cancelled)

41. (Original) A system according to claim [[40]] 38, wherein the at least one transport

function further comprises a second model is used to represent a tissue transport

function $h_s(t)$ represented by a second model through the ROI.

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42. (Original) A system according to claim 41 wherein the processor means selects an arterial input function $AIF_a(t)$ in the vessel leading to the ROI by searching pixels taken of the contrast agent concentration data.

43. (Original) A system according to claim 42 wherein the processor means measures the contrast agent concentration $C(t)$ remaining in the ROI.

44. (New) A method according to claim 22 further comprising measuring the arterial input function $AIF_t(t)$ by identifying a further artery showing a delay relative to $AIF_a(t)$ and thereafter fitting the estimate for the arterial input function $AIF_t(t)$ to the measured

5    $AIF_t(t)$ in order to optimise parameters t_1 and σ_1.

45. (New) A method according to claim 44 further comprising determining a relative dispersion β_1 value and applying the value to all other pixels of the same subjects assuming a constant relative dispersion.

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46. (New) A method according to claim 45 further comprising determining a constant relative dispersion β_1 value for all subjects such that the arterial transport function $h_a(t)$ of claim 8 is described by variable parameter t_1 and constant β_1.

15 47. (New) A method according to claim 46 further comprising accounting for delay and dispersion by:

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(i)   deriving an initial impulse residue function $R_0(t)$ by deconvolution of

AIF$_a$(t) from C(t);

(ii)   determining t_1 by the maximum position of $R_0(t)$;

(iii)   deriving the arterial input function AIF$_t$(t) of the vessel at the entry to the

5   ROI from $h_a(t)$ of claim 8, t_1 and constant β_1 to determine σ_1; and

(iv)   determining an estimate of blood flow F_t and an estimate of the tissue IRF

$R_e(t)$ from the deconvolution of:

$$C(t) = (F_t / k_H) \, AIF_t(t) \otimes R_e(t)$$

where $k_H = (1-H_a)/(1-H_t)$ is a correction constant taking into account different

10   values of arterial hematocrit H_a and tissue hematocrit H_t since the contrast agent

remains in the extracellular fraction of blood (plasma); and

(v)   determining perfusion indices as mean transit time $MTT = \int_0^\infty R_e(t)dt$;

blood flow $BF = F_t$ and blood volume $BV = BF * MTT$.

48.   (New) A method according to claim 31 further comprising the step of scaling

15 AIF$_a$(t) to VIF$_a$(t) in order to minimize partial voluming effect from the AIF$_a$(t).

49.   (New) A method according to claim 1 further comprising the step of representing

$h_a(t)$ using a Gaussian function in the first model such that:

$$h_a(t) = \begin{cases} \dfrac{1}{A_1} e^{-(t-t_1)^2/2\sigma_1^2} & (t \geq t_1) \\[2mm] 0 & (t < t_1) \end{cases}$$

where $t_1 \geq 0$, $A_1 = \sqrt{2\pi}\,\sigma_1[1 + erf(t_1/\sqrt{2}\sigma_1)]/2$ and $erf(t) \equiv \dfrac{2}{\sqrt{\pi}}\displaystyle\int_0^t e^{-x^2} dx$ is the error

function, t_1 is the time taken for the contrast agent to move from the initial

measurement of arterial input function $AIF_a(t)$ to a vessel at the entry to the ROI, σ_1 is

related to the mean transit time and dispersion of $h_a(t)$.

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50. (New) A method according to claim 1 wherein the at least one transport function

further includes a tissue transport function $h_s(t)$ represented by a second model through

the ROI, the method further comprising the step of representing $h_s(t)$ using a Gaussian

function in the second model such that:

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$$h_s(t) = \begin{cases} \dfrac{1}{A_2} e^{-(t-t_2)^2/2\sigma_2^2} & (t \geq t_2) \\[3mm] 0 & (t < t_2) \end{cases}$$

where $t_2 \geq 0$, $A_2 = \sqrt{2\pi}\,\sigma_2[1 + erf(t_2/\sqrt{2}\sigma_2)]/2$ and $erf(t) \equiv \dfrac{2}{\sqrt{\pi}}\displaystyle\int_0^t e^{-x^2} dx$ is the

error function, t_2 and σ_2 are related to the mean transit time and dispersion of $h_s(t)$.

51. (New) A computer readable medium storing a program for deriving blood perfusion

indices for a region of interest (ROI) of a subject by directing a processor to carry out

the method steps of claim 1 apart from the step of administering a contrast agent to the

subject during a dynamic imaging scan.

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52. (New) A computer readable medium storing a program according to claim 36, the

program further directing the processor to retrieve raw image data from the dynamic

imaging scan of the subject after a contrast agent is administered to the subject.

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